



Original research

Corneal thickness measurements with Scheimpflug and slit scanning imaging techniques in keratoconus

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Abstract

Purpose: To determine the repeatability of corneal thickness measurements with Scheimpflug (Pentacam) and slit scanning (Orbscan) imaging techniques in different grades of keratoconus.

Methods: This study was conducted as a cross-sectional research. Imaging with Orbscan and Pentacam was performed on patients with different grades of keratoconus. With each device, 3 measurements were taken at 10 min intervals. Repeatability indices in different grades of keratoconus were calculated for each device.

Results: Seventy-four eyes of 42 keratoconus patients were enrolled. Repeatability index of central corneal thickness (CCT) measurements in keratoconus grade 1, 2, and 3, were 12.8, 9.9, and 24.2 with Pentacam, and 23.6, 26.3, and 59.3 with Orbscan, respectively. For the thinnest point, these figures were 9.6, 8.0, and 35.7 with Pentacam and 19.5, 16.6, and 26.8 with Orbscan, respectively.

The 95% limit of agreement (LOA) between Pentacam and Orbscan in measuring CCT and thinnest point in grade 1 were −25.5–47.7 mic and −33.3–32.8 mic, respectively. These results for grade 2 were −9.8–50.6 mic and −26.2–43.7 mic, respectively. In grade 3, 95% LoA were −20–64.6 mic and −31.4–60.5 mic, respectively.

Conclusions: The results of this study showed that although repeated measurements of the CCT with Orbscan and Pentacam are strongly correlated, repeatability values of CCT measurements significantly decrease at more advanced grades of keratoconus. In all keratoconus grades, repeatability of CCT measurements was better with Pentacam than Orbscan. These findings indicate that corneal thickness readings have less validity in patients with advanced keratoconus.

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Keywords: Corneal thickness; Orbscan; Pentacam; Keratoconus; Repeatability; Agreement

Introduction

Keratoconus is the most common ectatic corneal disorder which is associated with visual discomfort and complaints of reduced and blurry vision on account of irregular astigmatism and myopia.¹ Early detection of the disease can help monitor the progress of the disease and making timely decisions about the treatment process.² The corneal thickness is one of the important anatomic corneal parameters in the workup before

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corneal refractive procedures, diagnosis of corneal ectasia especially early grades of keratoconus, follow-up of disease process, differential diagnosis, and assessing treatment effectiveness.

One of the most evident characteristics of keratoconus is non-inflammatory corneal thinning. In this disorder, the measurement of the corneal thickness is essential for the diagnosis, staging, monitoring, and proper planning for surgical treatment.³ Ultrasound pachymetry is the known gold standard for measuring central corneal thickness (CCT)⁴ which has limitations such as being invasive, fixation error, and error due to incorrect placement of the probe^{5,6}; therefore, other devices based on technologies such as Scheimpflug imaging (Pentacam), slit scanning topography (Orbscan), specular microscopy, dual-beam partial coherence interferometry, optical coherence tomography (OCT), and ultrasound biomicroscopy⁷ have found clinical applications.^{8,9} Repeatability is a requirement for device validity. In the assessment of accuracy, the first parameter which can be relied on is repeatability. Since a variety of devices are commonly used for corneal assessments in different clinical settings, it is important to have knowledge of their accuracy and repeatability.¹⁰ In keratoconus, corneal thinning and irregularity may be associated with reduced reproducibility and repeatability, and therefore, reduced accuracy of thickness readings with different techniques.¹¹ In addition, in follow-up of keratoconus patients, it is best to have minimum intra-examiner and inter-examiner variability. In clinical examinations and monitoring the disease progress, the corneal thickness is measured several times to obtain the best image quality and reduce error, and in certain cases, measurements are repeated by different examiners. Studies in this area are subject to greater imaging error in keratoconus patients compared to healthy subjects.¹²

An important limitation of previous studies is that device repeatability was not studied within different stages of keratoconus.^{3,13,14} Here, we present intra-examiner repeatability of corneal thickness measurements with Scheimpflug and slit scanning imaging techniques in different grades of keratoconus.

Methods

In this cross-sectional study, samples were selected keratoconic patients of the Noor Eye Hospital Keratoconus Clinic in Tehran. The sampling frame was the list of all patients who had a visit over the previous three months. In other words, we retrospectively reviewed the charts and then prospectively called the patients to come and participate. After selecting patients, the objectives and procedures of this project were explained to them, and signed consents were obtained from those willing to participate. Exclusion criteria were a history of ocular surgery, contact lens wear within the last month, ptosis, corneal abrasion or scar, and pterygium.

The Ethics Committee of Tehran University of Medical Sciences approved the study protocol, which was conducted in accord with the tenets of the Declaration of Helsinki. All participants signed a written informed consent.

Enrolled patients underwent imaging with Pentacam HR (Oculus, Wetzlar, Germany, software version 1.17r72) and Orbscan II (Bausch & Lomb, Orbtex Inc, Utah, USA) by a skilled optometrist. With each device, 3 readings were obtained at 10 min intervals. In case of error indicating insufficient image quality, imaging was repeated after 5 min. All imaging acquisitions were done between 10 a.m. and 3 p.m. The first measurement was done with Pentacam HR which is a high resolution computerized topography system that utilizes a digital rotating Scheimpflug camera. Data is collected from 25,000 points on the corneal surface, which is used to generate a three-dimensional image of the anterior cornea and provide elevation, curvature, and thickness maps. It also provides simulated k-readings of the flat and steep axes of the cornea which are equivalent to minimum and maximum keratometry readings, respectively. Imaging with Orbscan II was done next. With this device, which is based on the slit scanning technique, slit beams and back scattered light are used for triangulation and measuring the elevation of different points on the corneal surface relative to a reference surface. Twenty slit images are acquired in 0.7 s by scanning the cornea from limbus to limbus in both directions (a total of 40 images). At the same time, saccadic movements of the eye are tracked and taken into account in computations. Orbscan is capable of imaging the anterior and posterior corneal surfaces, the anterior surface of the iris, and the anterior chamber.

Statistical analysis

All data were entered in the Statistical Package for Social Sciences (SPSS) Version 20.0 (Chicago, IL, USA) for analysis. Variables extracted from each device included the thickness at the center and thinnest point of the cornea. Means and standard deviations of these variables were determined for each of the three measurements with each device in different grades of keratoconus.

Considering the previous studies that showed the Pentacam had a better agreement in the measurement of the central corneal thickness than ultrasound, we used the results of the Pentacam for grading keratoconus. Patients were grouped based on their maximum keratometry (kmax); <50.0 diopters (D) as group 1, $50.0 \text{ D} \leq kmax \leq 55.0 \text{ D}$ as group 2, and $>55.0 \text{ D}$ as group 3.¹⁵ First, the three measurements were compared using repeated measures analysis of variance controlling for the effect of the contralateral eye as a covariate. Then the intra-session test-retest variability was determined. After calculating the within-subjects standard deviation, we multiplied it by 2.77 to determine the repeatability index.¹⁶ The repeatability index (RI) also referred to as the Smallest Real Difference (SRD) is an indicator of repeated measurement error. The RI of a tool is directly related to the 95% limits of agreement¹⁷ proposed by Bland and Altman that contain 95% of differences between repeated measurements on the same subjects. The RI is the value below which the absolute differences between two measurements would lie with 0.95 probability. It is calculated by multiplying the within-subject standard deviation (S_w) or the Standard Error

Table 1

The mean and standard deviation (SD) of central corneal thickness (CCT) in three measurements and repeatability measurements obtained with Pentacam and Orbscan

CCT (micron)	First	Second	Third	RI	p-value*	ICC
Pentacam						
Grade 1	496.6 ± 32.91	497 ± 32.17	497.5 ± 32.67	12.8	0.758	0.979
Grade 2	459.92 ± 39.55	461.69 ± 40.75	462.69 ± 39.28	9.9	0.015	0.993
Grade 3	433.29 ± 29.53	428.94 ± 41.03	431.88 ± 37.79	24.2	0.742	0.943
Orbscan						
Grade 1	487.85 ± 43.46	485.81 ± 40.17	481 ± 42.6	23.6	0.178	0.958
Grade 2	443.78 ± 50.77	442.19 ± 45.87	440.78 ± 47.32	26.3	0.480	0.960
Grade 3	413.25 ± 55.74	413.25 ± 53.8	428.25 ± 51.65	59.3	0.286	0.849

RI: Repeatability.

ICC: Intraclass Correlation Coefficient.

*The p-value was calculated by repeated measure ANOVA.

of Measurement (SEM) by 2.77. The lower the index, the better the repeatability. To determine the coefficient of variation (CV), standard deviation was divided by the average of the measurements and expressed as percentages. A lower value is more desirable with this index as well. To examine the variance among repeated data, we determined the intraclass correlation coefficient (ICC). An ICC value of 1 means there is no difference in the variance of repeated data. An ICC value less than 0.75 is indicative of a weak correlation, while strong correlations generate values between 0.75 and 0.9. To compare means, we performed the repeated measures analysis of variance. Changes were considered significant based on a significance level of 5%. To demonstrate inter-device agreement, 95% limits of agreement (LoA) was used. The 95% LoA was calculated as “Mean ± 1.96 × standard deviation” of the inter-device difference.

Results

In this study, 74 eyes of 42 keratoconic patients were included; 30 grade-1 eyes, 26 grade-2 eyes, and 18 grade-3 eyes.

The mean age of these patients was 27.5 ± 6.1 years. 20 subjects were female, and 22 were male.

Table 1 summarizes central corneal thickness readings obtained from the three repeated measurements. Significant differences in repeated CCT readings were only seen with

Pentacam in grade-2 eyes, and other repeat measurements showed no statistically significant differences. In all three grades of keratoconus, Pentacam showed better repeatability than Orbscan; however, as demonstrated, repeatability decreased with both devices at more advanced grades of keratoconus.

Thickness measurements at the thinnest point with the two devices are presented in Table 2. Repeated measures analysis of variance showed no significant differences in measurements of the thinnest point with each of the two devices in the three levels of keratoconus. Repeatability with both devices decreased at more advanced stages of keratoconus.

Agreement of Pentacam and Orbscan

Table 3 shows the correlation and agreement between these two devices in terms of the grades of keratoconus. The correlation between Pentacam and Orbscan was quite high for CCT and thinnest point in grades of keratoconus. In grade 3, the highest bias (average inter-device difference in measuring corneal thickness) was seen between Pentacam and Orbscan.

Discussion

The objective of this study was to measure and compare the repeatability of readings with Pentacam and Orbscan II. Currently, a variety of contact and non-contact devices are

Table 2

The mean and standard deviation (SD) of corneal thinnest thickness in three measurements and repeatability measurements obtained with Pentacam and Orbscan

Thinnest point (micron)	First	Second	Third	RI	p-value*	ICC
Pentacam						
Grade 1	480.87 ± 32.6	480.90 ± 32.42	481.67 ± 32.88	9.6	0.569	0.988
Grade 2	440.96 ± 37.05	440.46 ± 37.66	441.46 ± 36.35	8.0	0.468	0.994
Grade 3	409.43 ± 30.97	403.06 ± 39.69	399.06 ± 37.48	35.7	0.029	0.965
Orbscan						
Grade 1	482 ± 44.49	481.93 ± 43.35	480.27 ± 45.59	19.5	0.564	0.975
Grade 2	432.23 ± 50.26	432.42 ± 48.56	432.04 ± 48.93	16.6	0.937	0.984
Grade 3	385.47 ± 50.97	384.89 ± 50.3	389.94 ± 48.17	26.8	0.977	0.956

RI: Repeatability.

ICC: Intraclass Correlation Coefficient.

*The p-value was calculated by repeated measure ANOVA.

Table 3

Agreement between paired readings of the central corneal thickness (CCT), and thinnest point in microns with Pentacam and Orbscan

	Grade	Pentacam	Orbscan	r	p-value*	p-value**	95% limit of agreement	CV
		Mean \pm SD	Mean \pm SD					
CCT (micron)	1	496.83 \pm 30.39	485.7 \pm 41.91	0.915	<0.001	0.005	–25.5 to 47.7	3.09
	2	462.64 \pm 39.37	442.25 \pm 47.39	0.954	<0.002	0.000	–9.8 to 50.6	3.97
	3	440.58 \pm 35.02	418.25 \pm 50.97	0.941	<0.003	0.022	–20.0 to 64.6	4.96
Thinnest point (micron)	1	481.14 \pm 32.5	481.40 \pm 44.11	0.948	<0.001	0.934	–33.3 to 32.8	2.43
	2	440.96 \pm 36.94	432.23 \pm 48.99	0.952	<0.002	0.019	–26.2 to 43.7	3.17
	3	400.06 \pm 36.17	385.50 \pm 49.09	0.892	<0.003	0.017	–31.4 to 60.5	4.87

r: correlation coefficient.

*p-value of correlation coefficient.

**p-value of paired t test.

CV: coefficient of variation.

available for the measurement of CCT, among which, Pentacam and Orbscan are the most common and most available. In light of novel treatment interventions such as intrastromal ring segment implantation,^{16,18–21} collagen cross-linking,²² and lamellar keratoplasty,²³ there is growing importance to determine the accuracy and repeatability with these techniques for measuring CCT in Keratoconus.² Therefore, it is essential to have knowledge about the repeatability of readings with these two devices in different grades of keratoconus.

Several studies have shown that central thickness measurements in normal eyes can be comparable between ultrasound and Orbscan provided that an appropriate correction factor is applied.^{24,25} However, this is the first study to examine the repeatability of central thickness readings with two of the most common non-contact methods at three different grades of keratoconus.

Similar to Orbscan, repeatability with Pentacam was reduced in keratoconus grade 3 compared to grades 1 and 2. In grade 3 keratoconus, although Pentacam is more repeatable than Orbscan, neither device has high repeatability.

Regarding CCT measurements, as demonstrated, Pentacam showed better reproducibility than Orbscan in all grades of keratoconus. However, the common finding between both Pentacam and Orbscan was decreased repeatability at higher grades of keratoconus. As presented in Table 1, the repeatability with both devices was significantly lower in grade 3 keratoconus compared to grades 1 and 2 of the disease.

In keratoconus with irregular and ectatic cornea and central opacity, the light may not penetrate the entire corneal thickness uniformly by scanning slit technology. The difference between the observed position of the posterior slit profile and the actual position of the posterior corneal surface can explain the artifactual pseudo ectasia images and lower pachymetry readings compared with Visante, RTVue, and ultrasound pachymeters.²⁶ Also, epithelial edema, changes in corneal water content, and extracellular matrix metabolism of the corneal stroma are other reasons for the underestimated CCT readings with Orbscan compared with ultrasound pachymetry.²⁷

de Sanctis et al have suggested that in keratoconic eyes, CCT measurements with rotating Scheimpflug camera is more repeatable than ultrasound pachymetry.³ This is because

rotating Scheimpflug camera automatically detects the corneal apex, measurement alignment is not dependent on the examiner, and repeatability with this method only depends on correct patient gaze. The difference between CCT measurements generated from ultrasound pachymetry and rotating Scheimpflug camera increases at higher grades of the disease, and readings tend to be lower with rotating Scheimpflug camera.

The results of this study showed that despite a high correlation between repeated CCT measurements with Pentacam or Orbscan, CCT repeatability significantly decreased at higher grades of keratoconus. In all grades of keratoconus, reproducibility of CCT measurements was better with Pentacam compared to Orbscan.

Our study showed that despite the strong correlation between corneal thickness measurement readings with Pentacam and Orbscan, the inter-device difference was statistically significant. According to previous studies on normal eyes,^{28,29} the two devices are in strong agreement and correlation in measuring the central corneal thickness. Nonetheless, a comparison of the limits of agreement between these two devices in studies of the central corneal thickness of normal eyes indicates lower levels of agreement in cases of keratoconus and that readings are not interchangeable in keratoconus patients.^{28–31} This is especially true in more advanced cases of keratoconus. Some previous studies have suggested that these two devices are non-interchangeable in cases of keratoconus,² although they are interchangeable in normal cases.

Although the results of this study are in favor of Pentacam reliability, it must be noted that both devices have low repeatability in patients with advanced keratoconus; therefore, results should be used with caution to avoid judgment error in diagnostic and therapeutic decisions.

The limitations of this study include a small sample size and lack of ultrasonography data, which is considered the gold standard for corneal thickness measurements, and absence of a normal control group.

In conclusion, corneal thickness repeatability is acceptable in normal people; however, the few reports concerning keratoconus patients are contradictory. This study showed that measurements of corneal thickness with Pentacam and Orbscan are less reliable in cases with severe keratoconus, and

measurements with Pentacam may be more repeatable. Moreover, the measurements from the two devices can not be used interchangeably.

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